L2

(FILE 'HOME' ENTERED AT 14:33:03 ON 27 JAN 2005)

FILE 'EMBASE, BIOSIS, MEDLINE, SCISEARCH, CAPLUS' ENTERED AT 14:33:18 ON 27 JAN 2005

L1 373 S HAIRPIN AND RNA AND LIBRARY

852 S (RIBOZYME OR SINGLE-STRANDED HAIRPIN RNA) AND LIBRARY

L3 1150 S L1 OR L2

L4 106738 S INHIBIT AND EXPRESSION AND GENE

L5 35 S L3 AND L4

L6 9 S VARIEGATED AND LIBRARY AND (RNA OR RIBOZYME)

L7 25 DUP REM L5 (10 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 14:38:30 ON 27 JAN 2005

FILE 'BIOSIS, MEDLINE, SCISEARCH, CAPLUS' ENTERED AT 14:45:44 ON 27 JAN 2005

L8 7 DUP REM L6 (2 DUPLICATES REMOVED)

FILE 'EMBASE, BIOSIS, MEDLINE, SCISEARCH, CAPLUS' ENTERED AT 14:46:02 ON 27 JAN 2005

FILE 'BIOSIS, MEDLINE, SCISEARCH, CAPLUS' ENTERED AT 14:46:02 ON 27 JAN 2005

FILE 'EMBASE, BIOSIS, MEDLINE, SCISEARCH, CAPLUS' ENTERED AT 14:49:13 ON 27 JAN 2005

FILE 'BIOSIS, MEDLINE, SCISEARCH, CAPLUS' ENTERED AT 14:49:14 ON 27 JAN 2005

L9 8 S SMALL (W) INTERFER? (W) RNA (W) LIBRAR?

L10 6 DUP REM L9 (2 DUPLICATES REMOVED)

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FILE 'MEDLINE' ENTERED AT 14:33:18 ON 27 JAN 2005

FILE 'SCISEARCH' ENTERED AT 14:33:18 ON 27 JAN 2005 Copyright (c) 2005 The Thomson Corporation.

FILE 'CAPLUS' ENTERED AT 14:33:18 ON 27 JAN 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> s hairpin AND rna AND library 373 HAIRPIN AND RNA AND LIBRARY

=> s (ribozyme or single-stranded hairpin rna) AND library 852 (RIBOZYME OR SINGLE-STRANDED HAIRPIN RNA) AND LIBRARY

=> s 11 or 12 1150 L1 OR L2

=> s inhibit AND expression AND gene 106738 INHIBIT AND EXPRESSION AND GENE

=> s 13 AND 14 35 L3 AND L4

=> s variegated AND library AND (rna or ribozyme) 9 VARIEGATED AND LIBRARY AND (RNA OR RIBOZYME)

=> dup rem 15 PROCESSING COMPLETED FOR L5 25 DUP REM L5 (10 DUPLICATES REMOVED)

=> d ibib ab 17 1-25

ANSWER 1 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

2004:1020024 CAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 141:421013

TITLE: Small interfering RNA libraries

and methods of cloning and use INVENTOR(S): Nichols, Mark; Steinman, Richard

PATENT ASSIGNEE(S): University of Pittsburgh of the Commonwealth System of

Higher Education, USA SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	ENT	NO.			KIN	D	DATE		i	APPL	I CAT	ION I	NO.		D	<b>ATE</b>	
			<b>-</b>			-					<del>-</del>						
WO	WO 2004101788				A2		2004	1125	1	WO 20	004-1	US14	494		. 20	0040	510
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, ÚA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRIORITY APPLN. INFO.: US 2003-469169P P 20030509

In one aspect, the invention provides a random or semirandom siRNA (encoding) library. Another aspect of the invention pertains to methods for construction of random or semirandom siRNA (encoding) libraries. Another aspect of the invention is vector systems for use in constructing siRNA libraries and/or that can express single siRNAs and siRNA libraries both constitutively and in an inducible fashion. In another aspect, the invention provides a method of using an siRNA library. The siRNA library is introduced into a population of cells. The population of cells then is subjected to a selection process to select a subpopulation of cells exhibiting a different behavioral, biochem., chemical, functional, mol., morphol., phenotypic, or phys. property from the remainder of population. Following the selection process, the subpopulation of cells can be isolated, analyzed, and/or cloned as desired. Such anal. of the subpopulation can be identification and sequencing of the siRNA species responsible for the different properties of the subpopulation relative to the remainder of the population. Alternatively, the subpopulation can be further analyzed by genomic, proteomic, and/or cellomic assays. Where such genomic, proteomic, and/or cellomic assays are employed, the method can produce several useful bioinformatics products. Specific siRNAs identified through this process may have direct therapeutic value. The invention claims RNA sequences for four siRNAs that inhibit human estrogen receptor a. In an example, a human cDNA library is digested into 100-1000 bp fragments using a restriction enzyme and cloned into plasmids having bidirectional transcription driven by flanking, oppositely-oriented T7 promoters. plasmids also have vaccinia E3L gene cloned in cis with the digested cDNA fragment. The resulting siRNA library is a population of plasmids, each containing a sense and antisense copy of a random 19-mer. In mammalian cells, transcription of the library will produce dsRNA and expression of the E3L protein will inhibit the interferon response to long dsRNAs and prevent cell death. The endogenous DICER enzyme will process the long dsRNAs into 21-23 bp siRNAs.

ANSWER 2 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN L7

ACCESSION NUMBER: 2004:430965 CAPLUS

DOCUMENT NUMBER: 141:2297

TITLE: Method for the synergistic gene silencing at

> both transcription level (using zinc finger protein) and post-transcription level (RNAi technologies), and

therapeutic uses

INVENTOR(S): Kim, Jin-Soo; Shin, Hyun Chul; Kwon, Heung-Sun

PATENT ASSIGNEE(S): Toolgen, Inc., S. Korea SOURCE: PCT Int. Appl., 75 pp.

CODEN: PIXXD2

Patent

DOCUMENT TYPE:

English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND APPLICATION NO. PATENT NO. DATE DATE

```
20040527
                                            WO 2003-KR2451
     WO 2004044202
                          A1
                                                                    20031114
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
             NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
             TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
N. INFO.: KR 2002-70845 A 20021114
PRIORITY APPLN. INFO.:
     The present invention relates to methods and compns. for regulating a
     target gene at both transcriptional and post-transcriptional
     levels. More particularly, it includes in one embodiment, a method for
     regulating a target gene, which comprises introducing into a
     cell a zinc finger protein binding to a promoter of the target
     gene or a DNA encoding said protein, and a RNA mol.
     binding to an mRNA transcribed from the target gene to
     inhibit the expression of said target gene. A
     composition for regulating a target gene comprising the zinc finger
     protein or a DNA encoding same, and the RNA mol. provide a
     substantially complete gene regulating effect due to the
     synergistic effect of the combination of ZFP and RNAi technologies.
REFERENCE COUNT:
                         3
                               THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 3 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                         2004:120982 CAPLUS
DOCUMENT NUMBER:
                         140:176309
TITLE:
                         Protein and cDNA sequences of human and mouse
                         cartilage differentiation inhibiting gene,
                         their therapeutic and diagnostic uses for cartilage
                         related diseases
INVENTOR(S):
                         Muramatsu, Shuji; Matsuda, Akio; Honda, Goichi
PATENT ASSIGNEE(S):
                         Asahi Kasei Kabushiki Kaisha, Japan
                         PCT Int. Appl., 306 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
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PAT	PATENT NO.				KIN	D :	DATE		i	APPL:	ICAT:	ION 1	NO.		Di	ATE	
WO	2004	0133	<del></del> 26		A1	-	2004	0212	,	WO 2	003-	JP99:	 39		20	0030	305
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NI,	NO,	ΝZ,	OM,
		PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	ΤJ,	TM,	TN,
		TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW			
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG
PRIORITY	IORITY APPLN. INFO.:									JP 2	002-2	2280	45	i	A 20	0020	305

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

AB The present invention provides protein and cDNA sequences of human and mouse cartilage differentiation inhibiting proteins that inhibit type II collagen expression, and their uses in diagnosis, treatment and prevention of diseases associated with cartilage impairments.

US 2002-401774P

P 20020808

Using the plasmid CPE43, the cDNA encoding a protein that can inhibit type II collagen expression is cloned from the cDNA library constructed from mouse cell line ATDC5 and human lung fibroblast, and the DNA sequence and the deduced amino acid sequence are determined The protein, the DNA encoding the protein, a recombinant vector containing the DNA, and a transformant containing the recombinant vector are useful in screening for a substance inhibiting or promoting the type II collagen expression.

L7 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:101279 CAPLUS

DOCUMENT NUMBER:

140:158524

TITLE:

Partially double stranded RNAs with hairpin structures for use in RNA interference without induction of RNA

-associated toxicity and their therapeutic uses

INVENTOR(S):

Pachuk, Catherine J.; Satishchandran, C.; Chopra,

THACHIOK(2).

Maninder; Shuey, David Nucleonics, Inc., USA

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 174 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	PATENT NO.					D .	DATE		1	APPL	ICAT:	ION	NO.		D	ATE	
						-											
WO	2004	0116	24		A2		2004	0205	1	WO 2	003-1	US24	028		2	0030	731
WO	2004	0116	24		C2		2004	0408									
WO	2004	0116	24		A3		2004	1209									
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	ΜA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	OM,
		PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	ТJ,	TM,	TN,
		TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW			
	RW:	GH,	GM,	KE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
PRIORIT	RIORITY APPLN. INFO.:								1	JS 2	002-	3999	98P	]	P 2	0020	731
AB Pa:	B Partially double					ed i	nter	feri	ng R	NAs	that	inc	lude	a			

Partially double-stranded interfering RNAs that include a hairpin structure are described for use in RNA interference. These interfering RNAs specifically inhibit the expression of target genes in a cell or animal without inducing the toxic effects, such as the RNA stress response, seen with prior art interfering RNAs. These methods can be used to prevent or treat a disease or infection by silencing a gene associated with the disease or infection. The invention also provides methods for identifying nucleic acid sequences that modulate a detectable phenotype, such as the function of a cell, the expression of a gene, or the biol. activity of a target polypeptide.

L7 ANSWER 5 OF 25 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN DUPLICATE 1

ACCESSION NUMBER:

2004493962 EMBASE

TITLE:

Identification of cellular cofactors for human immunodeficiency virus replication via a ribozyme

-based genomics approach.

AUTHOR:

Waninger S.; Kuhen K.; Hu X.; Chatterton J.E.; Wong-Staal

F.; Tang H.

CORPORATE SOURCE: H. Tang, Department of Biological Sciences, Biology Unit 1,

Florida State University, Tallahassee, FL 32306-4370,

United States. tang@bio.fsu.edu

SOURCE: Journal of Virology, (2004) 78/23 (12829-12837).

Refs: 35

ISSN: 0022-538X CODEN: JOVIAM

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology

026 Immunology, Serology and Transplantation

LANGUAGE: English SUMMARY LANGUAGE: English

Ribozymes are small, catalytic RNA molecules that can be engineered to down-regulate gene expression by cleaving specific mRNA. Here we report the selection of hairpin ribozymes that inhibit human immunodeficiency virus (HIV) replication from a combinatorial ribozyme library . We identified a total of 17 effective ribozymes, each capable of inhibiting HIV infection of human CD4 (+) cells. These ribozymes target diverse steps of the viral replication cycle, ranging from entry to transcription. One ribozyme suppressed HIV integration and transcription by inhibiting the expression of the Ku80 subunit of the DNA-activated protein kinase. Another ribozyme specifically inhibited long terminal repeat transactivation, while two additional ones blocked a step that can be bypassed by vesicular stomatitis virus G-protein pseudotyping. The function of Ku80 in HIV replication and its mechanism of action were further confirmed using short interfering RNA. Identification of the gene targets of these and other selected ribozymes

L7 ANSWER 6 OF 25 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on

STN

ACCESSION NUMBER: 2004:653333 SCISEARCH

THE GENUINE ARTICLE: 837QY

TITLE: Aminoglycoside microarrays to explore interactions of

may reveal novel therapeutic targets for combating HIV infection.

antibiotics with RNAs and proteins

AUTHOR: Disney M D; Seeberger P H (Reprint)

CORPORATE SOURCE: ETH Honggerberg, Organ Chem Lab, Swiss Fed Inst Technol,

HCI F315, CH-8093 Zurich, Switzerland (Reprint); ETH Honggerberg, Organ Chem Lab, Swiss Fed Inst Technol, CH-8093 Zurich, Switzerland; MIT, Dept Chem, Cambridge, MA

02139 USA

COUNTRY OF AUTHOR: Switzerland; USA

SOURCE: CHEMISTRY-A EUROPEAN JOURNAL, (5 JUL 2004) Vol. 10, No.

13, pp. 3308-3314.

Publisher: WILEY-V C H VERLAG GMBH, PO BOX 10 11 61,

D-69451 WEINHEIM, GERMANY.

ISSN: 0947-6539. Article; Journal

DOCUMENT TYPE: Article LANGUAGE: English

REFERENCE COUNT: 63

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

RNA is an important target for drug discovery efforts. Several clinically used aminoglycoside antibiotics bind to bacterial rRNA and inhibit protein synthesis. Aminoglycosides, however, are losing efficacy due to their inherent toxicity and the increase in antibiotic resistance. Targeting of other RNAs is also becoming more attractive thanks to the discovery of new potential RNA drug targets through genome sequencing and biochemical efforts. Identification of new compounds that target RNA is therefore urgent, and we report here on the development of

rapid screening methods to probe binding of low molecular weight ligands to proteins and RNAs. A series of aminoglycosides has been immobilized onto glass microscope slides, and binding to proteins and RNAs has been detected by fluorescence. Construction and analysis of the arrays is completed by standard DNA genechip technology. Binding of immobilized aminoglycosides to proteins that are models for study of aminoglycoside toxicity (DNA polymerase and phospholipase C), small RNA oligonucleotide mimics of aminoglycoside binding sites in the ribosome (rRNA A-site mimics), and a large (approximate to 400 nucleotide) group I ribozyme RNA is detected. The ability to screen large RNAs alleviates many complications associated with binding experiments that use isolated truncated regions from larger RNAs. These studies lay the foundation for rapid identification of small organic ligands from combinatorial libraries that exhibit strong and selective RNA binding while displaying decreased affinity to toxicity-causing proteins.

L7 ANSWER 7 OF 25 MEDLINE on STN DUPLICATE 2

2004256536 ACCESSION NUMBER: MEDLINE DOCUMENT NUMBER: PubMed ID: 15119963

TITLE: A plasmid-based system for expressing small interfering

> RNA libraries in mammalian cells. Kaykas Ajamete; Moon Randall T

CORPORATE SOURCE: Howard Hughes Medical Institute, Department of

Pharmacology, and Center for Developmental Biology,

University of Washington School of Medicine, Seattle, WA

98195,. USA.akaykas@u.washington.edu

SOURCE: BMC cell biology [electronic resource], (2004 Apr 30) 5 (1)

Journal code: 100966972. ISSN: 1471-2121.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

AUTHOR:

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200406

ENTRY DATE: Entered STN: 20040525

Last Updated on STN: 20040602 Entered Medline: 20040601

AΒ BACKGROUND: RNA interference (RNAi) is an evolutionarily conserved process that functions to inhibit gene expression. The use of RNAi in mammals as a tool to study gene function has rapidly developed in the last couple of years since the discovery that the function-inhibiting units of RNAi are short 21-25 nt double-stranded RNAs (siRNAs) derived from their longer template. The use of siRNAs allows for gene-specific knock-down without induction of the non-specific interferon response in mammalian cells. Multiple systems have been developed to introduce siRNAs into mammals. One of the most appealing of these techniques is the use of vectors containing polymerase III promoters to drive expression of hairpin siRNAs. However, there are multiple limitations to using hairpin siRNA vectors including the observation that some are unstable in bacteria and are difficult to sequence. RESULTS: To circumvent the limitation of hairpin siRNA vectors we have developed a convergent opposing siRNA expression system called pHippy. We have generated pHippy vectors or expression cassettes that knock down the expression of both reporter and endogenous genes. As a proof of principle that pHippy can be used to generate random siRNA libraries, we generated a small siRNA library against PGL3 luciferase and demonstrated that we could recover functional siRNAs that knock down PGL3 luciferase. CONCLUSIONS: siRNA is a powerful tool to study gene function. We have developed a new vector with opposing convergent promoters for the expression of siRNAs, which can be used to knock down endogenous

genes in a high throughput manner or to perform functional screening with random or cDNA-derived siRNA libraries.

ANSWER 8 OF 25 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

ACCESSION NUMBER:

2004531391 EMBASE

A plasmid-based system for expressing small interfering TITLE:

RNA libraries in mammalian cells.

Kaykas A.; Moon R.T. AUTHOR:

CORPORATE SOURCE: R.T. Moon, Howard Hughes Medical Institute, Department of

Pharmacology, Univ. of Washington School of Med., Seattle,

WA 98195, United States. rtmoon@u.washington.edu

BMC Cell Biology, (30 Apr 2004) 5/- (11p). SOURCE:

Refs: 23

ISSN: 1471-2121 CODEN: BCBMAY

COUNTRY: United Kingdom Journal; Article DOCUMENT TYPE:

FILE SEGMENT: 022 Human Genetics

> 029 Clinical Biochemistry

LANGUAGE: English SUMMARY LANGUAGE: English

Background: RNA interference (RNAi) is an evolutionarily

conserved process that functions to inhibit gene

expression. The use of RNAi in mammals as a tool to study gene function has rapidly developed in the last couple of years

since the discovery that the function-inhibiting units of RNAi are short

21-25 nt double-stranded RNAs (siRNAs) derived from their longer template. The use of siRNAs allows for gene-specific knock-down without induction of the non-specific interferon response in mammalian

cells. Multiple systems have been developed to introduce siRNAs into mammals. One of the most appealing of these techniques is the use of vectors containing polymerase III promoters to drive expression

of hairpin siRNAs. However, there are multiple limitations to using hairpin siRNA vectors including the observation that some are unstable in bacteria and are difficult to sequence. Results: To circumvent the limitation of hairpin siRNA vectors we have

developed a convergent opposing siRNA expression system called pHippy. We have generated pHippy vectors or expression cassettes that knock down the expression of both reporter and endogenous

genes. As a proof of principle that pHippy can be used to generate random siRNA libraries, we generated a small siRNA

library against PGL3 luciferase and demonstrated that we could recover functional siRNAs that knock down PGL3 luciferase. Conclusions: siRNA is a powerful tool to study gene function. We have

developed a new vector with opposing convergent promoters for the expression of siRNAs, which can be used to knock down endogenous

genes in a high throughput manner or to perform functional screening with random or cDNA-derived siRNA libraries. . COPYRGT.

2004 Kaykas and Moon; licensee BioMed Central Ltd.

L7 ANSWER 9 OF 25 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. STN DUPLICATE 3

ACCESSION NUMBER: 2004:320712 BIOSIS DOCUMENT NUMBER: PREV200400321938

TITLE: A plasmid-based system for expressing small interfering

RNA libraries in mammalian cells.

AUTHOR(S): Kaykas, Ajamete; Moon, Randall T. [Reprint Author] CORPORATE SOURCE: Howard Hughes Med InstDept Pharmacol, Univ Washington,

Seattle, WA, 98195, USA

akaykas@u.washington.edu; rtmoon@u.washington.edu

BMC Cell Biology, (April 30 2004) Vol. 5, No. April 30. SOURCE:

print.

ISSN: 1471-2121 (ISSN online).

DOCUMENT TYPE: Article LANGUAGE: English

ENTRY DATE: Entered STN: 21 Jul 2004

Last Updated on STN: 21 Jul 2004

Background: RNA interference (RNAi) is an evolutionarily conserved process that functions to inhibit gene expression. The use of RNAi in mammals as a tool to study gene function has rapidly developed in the last couple of years since the discovery that the function-inhibiting units of RNAi are short 21-25 nt double-stranded RNAs (siRNAs) derived from their longer template. The use of siRNAs allows for gene-specific knock-down without induction of the non-specific interferon response in mammalian cells. Multiple systems have been developed to introduce siRNAs into mammals. One of the most appealing of these techniques is the use of vectors containing polymerase III promoters to drive expression of hairpin siRNAs. However, there are multiple limitations to using hairpin siRNA vectors including the observation that some are unstable in bacteria and are difficult to sequence. Results: To circumvent the limitation of hairpin siRNA vectors we have developed a convergent opposing siRNA expression system called pHippy. We have generated pHippy vectors or expression cassettes that knock down the expression of both reporter and endogenous genes. As a proof of principle that pHippy can be used to generate random siRNA libraries, we generated a small siRNA library against PGL3 luciferase and demonstrated that we could recover functional siRNAs that knock down PGL3 luciferase. Conclusions: siRNA is a powerful tool to study gene function. We have developed a new vector with opposing convergent promoters for the expression of siRNAs, which can be used to knock down endogenous genes in a high throughput manner or to perform functional screening with random or cDNA-derived siRNA libraries.

L7 ANSWER 10 OF 25 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2004233749 MEDLINE DOCUMENT NUMBER: PubMed ID: 14604435

TITLE: Expressing functional siRNAs in mammalian cells using

convergent transcription.

AUTHOR: Tran Nham; Cairns Murray J; Dawes Ian W; Arndt Greg M

CORPORATE SOURCE: Johnson and Johnson Research Pty Ltd, 1 Central Ave,

Australian Technology Park, Eveleigh, NSW 1430, Australia..

nham@nucleics.com

SOURCE: BMC biotechnology [electronic resource], (2003 Nov 6) 3 (1).

21.

Journal code: 101088663. ISSN: 1472-6750.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200407

ENTRY DATE: Entered STN: 20040511

Last Updated on STN: 20040723 Entered Medline: 20040722

AB BACKGROUND: The use of small interfering RNAs (siRNAs) as genetic inhibitors of gene expression has been shown to be an effective way of studying gene function in mammalian cells. Recently, different DNA vectors for expression of small hairpin RNAs (shRNAs) or co-expression of sense and antisense RNAs have been developed that direct siRNA-mediated gene silencing. One expression cassette design that has been used to express long sense and antisense RNAs in non-mammalian cell types is symmetric transcription using

convergent promoters. However, convergent transcription as a way to generate functional siRNAs in mammalian cells has not been reported. This vector design permits the generation of expression constructs containing no repeat sequences, but capable of inducing RNA interference (RNAi)-mediated gene silencing. RESULTS: With the aim of simplifying the construction of RNAi expression vectors, we report on the production and application of a novel convergent promoter cassette capable of expressing sense and antisense RNAs, that form double-stranded RNA, and mediate gene silencing in mammalian cells. We use this cassette to inhibit the expression of both the EGFP transgene and the endogenous TP53 gene. The gene silencing effect is Dicer-dependent and the level of gene inactivation achieved is comparable to that produced with synthetic siRNA. Furthermore, this expression system can be used for both short and long-term control of specific gene expression in mammalian cells. CONCLUSION: The experiments performed in this study demonstrate that convergent transcription can be used in mammalian cells to invoke gene -specific silencing via RNAi. This method provides an alternative to expression of shRNAs and co-expression of sense and antisense RNAs from independent cassettes or a divergent promoter. The main advantage of the present vector design is the potential to produce a functional siRNA expression cassette with no repeat sequences. Furthermore, the cassette design reported is ideal for both routine use in controlling specific gene expression and construction of randomised RNAi expression libraries for use in unbiased forward genetic selections.

L7 ANSWER 11 OF 25 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004279008 EMBASE

TITLE: Expressing functional siRNAs in mammalian cells using

convergent transcription.

AUTHOR: Tran N.; Cairns M.J.; Dawes I.W.; Arndt G.M.

CORPORATE SOURCE: G.M. Arndt, Johnson/Johnson Research Pty Ltd., 1 Central

Ave., Eveleigh, NSW 1430, Australia. garndt@medau.jnj.com

SOURCE: BMC Biotechnology, (6 Nov 2003) 3/- (9p).

Refs: 34

ISSN: 1472-6750 CODEN: BBMIE6

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

029 Clinical Biochemistry

LANGUAGE: English SUMMARY LANGUAGE: English

Background: The use of small interfering RNAs (siRNAs) as genetic inhibitors of gene expression has been shown to be an effective way of studying gene function in mammalian cells. Recently, different DNA vectors for expression of small hairpin RNAs (shRNAs) or co-expression of sense and antisense RNAs have been developed that direct siRNA-mediated gene silencing. One expression cassette design that has been used to express long sense and antisense RNAs in nonmammalian cell types is symmetric transcription using convergent promoters. However, convergent transcription as a way to generate functional siRNAs in mammalian cells has not been reported. This vector design permits the generation of expression constructs containing no repeat sequences, but capable of inducing RNA interference (RNAi)-mediated gene silencing. Results: With the aim of simplifying the construction of RNAi expression vectors, we report on the production and application of a novel convergent promoter cassette capable of expressing sense and antisense RNAs, that

form double-stranded RNA, and mediate gene silencing in mammalian cells. We use this cassette to inhibit the expression of both the EGFP transgene and the endogenous TP53 gene. The gene silencing effect is Dicer-dependent and the level of gene inactivation achieved is comparable to that produced with synthetic siRNA. Furthermore, this expression system can be used for both short and long-term control of specific gene expression in mammalian cells. Conclusion: The experiments performed in this study demonstrate that convergent transcription can be used in mammalian cells to invoke gene -specific silencing via RNAi. This method provides an alternative to expression of shRNAs and co-expression of sense and antisense RNAs from independent cassettes or a divergent promoter. The main advantage of the present vector design is the potential to produce a functional siRNA expression cassette with no repeat sequences. Furthermore, the cassette design reported is ideal for both routine use in controlling specific gene expression and construction of randomised RNAi expression libraries for use in unbiased forward genetic selections. . COPYRGT. 2003 Tran et al; licensee BioMed Central Ltd.

ANSWER 12 OF 25 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on L7 STN DUPLICATE 5

ACCESSION NUMBER: 2004:72033 BIOSIS DOCUMENT NUMBER: PREV200400075343

TITLE: Expressing functional siRNAs in mammalian cells using

convergent transcription.

Tran, Nham; Cairns, Murray J.; Dawes, Ian W.; Arndt, Greg AUTHOR(S):

M. [Reprint Author]

CORPORATE SOURCE: Johnson and Johnson Research Pty Ltd., 1 Central Avenue,

Australian Technology Park, Eveleigh, NSW, 1430, Australia nham@nucleics.com; murray@nucleics.com; Idawes@unsw.edu.au;

garndt@medau.jnj.com

SOURCE:

BMC Biotechnology, (6 November 2003) Vol. 3, No. 21 Cited November 24, 2003. http://www.biomedcentral.com/content/pdf

/1472-6750-3-21.pdf. cited January 8, 2004. http://www.biomedcentral.com/1472-6750. online.

ISSN: 1472-6750 (ISSN online).

DOCUMENT TYPE: Article LANGUAGE: English

ENTRY DATE: Entered STN: 4 Feb 2004

Last Updated on STN: 4 Feb 2004

Background: The use of small interfering RNAs (siRNAs) as genetic inhibitors of gene expression has been shown to be an effective way of studying gene function in mammalian cells. Recently, different DNA vectors for expression of small hairpin RNAs (shRNAs) or co-expression of sense and antisense RNAs have been developed that direct siRNA-mediated gene silencing. One expression cassette design that has been used to express long sense and antisense RNAs in nonmammalian cell types is symmetric transcription using convergent promoters. However, convergent transcription as a way to generate functional siRNAs in mammalian cells has not been reported. This vector design permits the generation of expression constructs containing no repeat sequences, but capable of inducing RNA interference (RNAi)-mediated gene silencing. Results: With the aim of simplifying the construction of RNAi expression vectors, we report on the production and application of a novel convergent promoter cassette capable of expressing sense and antisense RNAs, that form double-stranded RNA, and mediate gene silencing in mammalian cells. We use this cassette to inhibit the expression of both the EGFP transgene and the endogenous TP53

The gene silencing effect is Dicer-dependent and the level of gene inactivation achieved is comparable to that produced with synthetic siRNA. Furthermore, this expression system can be used for both short and long-term control of specific gene expression in mammalian cells. Conclusion: The experiments performed in this study demonstrate that convergent transcription can be used in mammalian cells to invoke gene -specific silencing via RNAi. This method provides an alternative to expression of shRNAs and co-expression of sense and antisense RNAs from independent cassettes or a divergent promoter. The main advantage of the present vector design is the potential to produce a functional siRNA expression cassette with no repeat sequences. Furthermore, the cassette design reported is ideal for both routine use in controlling specific gene expression and construction of randomised RNAi expression libraries for use in unbiased forward genetic selections.

L7 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:575234 CAPLUS

DOCUMENT NUMBER: 137:136059

TITLE: Protein and cDNA sequences of Drosophila gene

Indy which encodes cellular carboxylate transporters

DAME

and its effects on longevity

INVENTOR(S): Rogina, Blanka; Reenan, Robert A.; Helfand, Stephen L.

PATENT ASSIGNEE(S): University of Connecticut, USA

SOURCE: PCT Int. Appl., 84 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

P.A	PATENT NO.					_	DATE		_	APPL.						ATE	
	2002				A2 A3		2002	0801								0011	
110									D A	DD	D.C	DD.	DV	D.C	C 3	CII	CNI
	w :						AU,										
							DK,										
		HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,
		LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,
		RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	UZ,	VN,
		YU,	ZA,	ZW													
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	KZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	CH,	CY,	DE,	DK,	ES,	FI,	FR,	GB,
		GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,
		GN,	GQ,	GW,	$\mathtt{ML}$ ,	MR,	ΝE,	SN,	TD,	TG							
CA	2431	517			AA		2002	0801	(	CA 2	001-	2431	517		2	0011	212
EP	EP 1399553						2004	0324	]	EP 20	001-	99422	21		2	0011	212
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
	IE, SI, LT					FI,	RO,	MK,	CY,	AL,	TR						
PRIORIT	RIORITY APPLN. INFO.:								1	US 20	000-2	2550:	13P	1	2 (	0001	212
									1	WO 2	001-	JS48	130	V	v 2	0011	212

AB This present invention discloses protein and cDNA sequences of Drosophila melanogaster gene Indy which encodes a cellular carboxylate transporter and its effects on longevity. Specifically, the invention discloses that gene Indy expresses in fat body, midgut and oenocytes in adult flies, its mutations have a pos. effect on life span, fertility and phys. activity. This disclosure also encompasses homologs of the Indy gene both from Drosophila and other organisms. In addition, this disclosure encompasses the use of Indy polynucleotides, INDY proteins and polypeptides, antibodies to the INDY protein, antagonists that inhibit Indy activity or expression, and agonists

that increase Indy activity or expression, in the diagnosis or treatment of body weight disorders or longevity in humans and animals.

ANSWER 14 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2002:11125 CAPLUS

DOCUMENT NUMBER:

136:49331

TITLE:

Random intracellular method for obtaining optimally

active nucleic acid molecules

INVENTOR(S):

Nilsen, Timothy W.; Robertson, Hugh D.; Kindt, Thomas

J.

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 17 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2002002278	A1	20020103	US 1999-434598	19991105
PRIC	DRITY APPLN. INFO.:			US 1999-434598	19991105
AB	Vectors and a method	od for t	he identifi	cation of affector RNA	A mols., such as
	ribozymes, externa	l guide	sequences,	anti-sense RNA, and to	riple
	helix-forming RNA,	that in	hibit expre	ession of target	-
	RNA mols. are disc	losed.	The method	identifies functional	affector RNA
	mols. by screening	or sele	ecting for t	those RNA mols. that in	nhibit
				nich includes the seque	
	an RNA mol. of inte	erest, i	from a <b>libr</b> a	ry of potential affect	tor
	RNA mols. The vect	tors ind	clude a repo	orter gene encoding the	e
				nol. of interest and R1	
				nclude a second report	
				Expression of the second	
				detect transformation	
				ntrol for effects on th	
				ein that are not due t	50
				nol. of interest. The	
				nol. targeted to the Ri	
				nod and vectors is the	
				interest in an in vi	
				nilar to the setting wh	
				advantage of the disc	
				the accessible sites	
				say. Also disclosed a	re affector oligomers
				ed as inhibiting the	
				ne disclosed method als	
	<del>_</del>			oitory activities of di	Liierent
	affector RNA mols.	directe	ed to differ	ent target sites.	

L7 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2001:816911 CAPLUS

DOCUMENT NUMBER:

135:367726

TITLE:

Cellular regulatory genes that support the

replication of infectious agents, and

ribozymes that target such cellular regulatory

genes, and methods of use

INVENTOR(S):

Kruger, Martin; Welch, Peter J.; Barber, Jack R.

Immusol, Incorporated, USA PCT Int. Appl., 74 pp. PATENT ASSIGNEE(S):

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

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PATENT NO.
                         KIND DATE
                                             APPLICATION NO.
                                                                      DATE
                          ____
                                              __________
     WO 2001083754
                         A2
                                 20011108
                                              WO 2001-US14337
                                                                      20010502
     WO 2001083754
                         . A3
                                 20021003
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 6808876
                                 20041026 US 2000-563794
                           В1
                                                                      20000502
     CA 2409219
                           AA
                                 20011108
                                           CA 2001-2409219
                                                                      20010502
                                 20030129
                                           EP 2001-932962
     EP 1278845
                           A2
                                                                      20010502
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.:
                                              US 2000-563794
                                                                   A1 20000502
                                              WO 2001-US14337
                                                                   W 20010502
     The invention is directed to methods of identifying cellular regulatory
AΒ
     genes that support the replication of viruses such as hepatitis C
     virus (HCV). The methods are directed to the identification of
     ribozymes that target such cellular regulatory genes and
     to identifying the genes targeted by the ribozymes.
     The invention provides ribozymes with target recognition
     sequences (N8-AGAA-N4) that allow the ribozyme to target and
     cleave cellular regulators. Also provided are nucleic acids encoding
     various cellular regulators and sequences in such nucleic acid for which
     ribozymes can be directed. Fragments of these nucleic acid and
     protein sequences also are provided. Further provided is a method for
     identifying a ribozyme reactive with a cellular regulator of
     viral replication or expression, and a method for identifying
     the cellular regulator targeted by such ribozymes. Also
     provided is a method of identifying a compound that modulates the activity
     of a cellular regulator. A selection system based on a randomized
     hairpin ribozyme gene library to
     identify cellular factors involved in HCV IRES function have been
     developed. A retroviral vector ribozyme library with
     randomized target recognition sequences was introduced into HeLa cells,
     stably expressing a bicistronic construct encoding the hygromycin B
     phosphotransferase gene and the herpes simplex virus thymidine
     kinase gene (HSV-tk). Translation of the HSV-tk gene
     was mediated by the HCV IRES. Cells expressing ribozymes that
     inhibit HCV IRES-mediated translation of HSV-tk were selected via
     their resistance to both ganciclovir and hygromycin B. Two
     ribozymes reproducibly conferred the ganciclovir-resistant
     phenotype and were shown to inhibit IRES-mediated translation of
     HCV core protein but did not inhibit cap-dependent protein
     translation or cell growth. The functional targets of these
     ribozymes were identified as the gamma subunits of human
     eukaryotic initiation factors (eIF2B\gamma) and (eIF2\gamma).
     involvement of eIF2By and eIF2y in HCV IRES-mediated
     translation was further validated by ribozymes directed against
     addnl. sites within the mRNAs of these genes. Two more cellular
     regulators were identifyed that correspond to a cellular proteasome
     complex. In addition to leading to the identification of cellular IRES
     cofactors, ribozymes obtained from this cellular selection
```

system could be directly used to specifically inhibit HCV viral

translation, thereby facilitating the development of new antiviral strategies for HCV infection.

L7 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2001:636271 CAPLUS

DOCUMENT NUMBER:

135:206427

TITLE:

Platform for the discovery of the bacterial genes involved in RNA modification, and

methods for screening for antibiotics Roberts, T. Guy; Mitchell, Wayne; Beckman, Kenneth

INVENTOR(S):
PATENT ASSIGNEE(S):

Montclair Group, USA PCT Int. Appl., 44 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

Engii

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.				KIN	D	DATE		4		ICAT				D	ATE		
	WO	2001	0629	81		A1	<del>-</del>	2001	0830	1						2	0010	223
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
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			HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,
			LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,
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			DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,
			ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG		
	CA	2401	018			AA		2001	0830	(	CA 2	001-	2401	018		2	0010	223
	US	2002	0018	04		A1		2002	0103	1	US 2	001-	7928	78		2	0010	223
	EP	1263	986			A1		2002	1211		EP 2	001-	9144	70		2	0010	223
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,
			ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR						
PRIO	RIT	APP	LN.	INFO	. :					1	US 2	000-	1850	00P	1	P 2	0000	225
										1	US 2	000-	1850	71P		P 20	0000	225
										1	US 2	000-2	2555	06P	1	P 2	0000	225
				1	US 2	000-2	2255	05P	1	P 2	0000	815						
										1	WO 2	001-1	US59:	20	1	W 2	0010	223
			_															

AB Methods for identifying genes and gene products involved in RNA modification, and methods for screening test compds. or antibiotics for activity are provided. The expression of a candidate 'test' gene is modulated within an organism and the product of the activity of interest is analyzed for similar modulation. If this activity is vital to the pathogenicity of an organism or a disease, then the identification of the responsible enzyme and its gene in the above manner serves to characterize a useful drug target. The present invention systemizes this process of drug target identification by providing methods for correlating mol. and cellular structures to their causative genes. Furthermore, this invention provides methods for the simultaneous discovery of classes of enzymes that share at least one substrate in common. Where the members of the chosen class of substrates, termed "sentinel mols.," can be modified by any of a number of catalytic mechanisms, the assay is not limited to a specific enzymic activity. When performed in a multi-well format, the methods employing these sentinel mols. can be performed in a high throughput fashion. Addnl., the gene products identified in the methods, the genes that encode the gene products, modified sentinel mols. produced by the gene products, and compds. or antibiotics which inhibit the modification process are provided.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 17 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

2000:646132 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

133:218523

TITLE:

Hybridization and selection methods for identification

of synthetic nucleic acid sequences capable of

inhibiting gene expression

INVENTOR(S):

Gyuris, Jeno

PATENT ASSIGNEE(S): SOURCE:

Mitotix, Inc., USA PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	PATENT NO.						DATE				ICAT				Ι	ATE	
WO	2000	0537	43				2000	0914							2	0000	310
	W:	ΑE,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,	CU,
		CZ,	DE,	DK,	DM,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,
		IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,
		MD,	MG,	MK,	MN,	MW,	ΜX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,
		SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW,	AM,
		ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM								
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		DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,
		CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG				
CA	2362	414			AA		2000	0914	(	CA 2	000-	2362	414		2	0000	310
EP	1161	528			A1	:	2001	1212	1	EP 2	000-	9162	59		2	0000	310
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					LV,		RO										
	6342				В1		2002	0129	Ţ	US 2	000-	5227	28		2	0000	310
JP	JP 2002537835						2002	1112		JP 2	000-	6033	64		2	0000	310
AU	AU 774332				В2		2004	0624	1	AU 2	000-	3739	0		2	0000	310
US	US 2003157477				<b>A</b> 1		2003	0821	τ	US 2	001-	9509	83		2	0010	912
PRIORIT	PRIORITY APPLN. INFO.:								τ	US 1	999-	1239	24P	I	? 1	.9990	312
									Ţ	US 2	000-	5227	28	1	A1 2	0000	310
									Ţ	WO 2	000-	JS63	85	V	v 2	0000	310

AB The present invention relates to a selection method that allows fast recovery and identification of functional gene fragments that selectively inhibit growth, e.g., are cytostatic or cytotoxic, of particular cell-types, such as transformed cells. The strategy relies, in part, on the ability of small gene fragments to encode dominant-acting synthetic genetic elements (SGEs), e.g., mols. which interfere with the function of genes from which they are derived. SGEs which can be identified by the subject method include, but are not limited to, inhibitory antisense RNA mols., ribozymes, nucleic acid decoys, and small peptides.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 18 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:191261 CAPLUS

DOCUMENT NUMBER:

132:232751

TITLE:

sequence and therapeutic applications for rat

pancreatic T-type calcium channel as it relates to

diabetes

INVENTOR(S):

Li, Ming

PATENT ASSIGNEE(S):

South Alabama Medical Science Foundation, USA

SOURCE: PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	PATENT NO.			KIN	D -	DATE			APPL	ICAT	ION I	NO.		D	ATE			
WO	2000	0158	45		A1	_	2000	0323	1	wo 1	999-1	US19	675		19	9990	826	
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		ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	
		CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG						
CA	2340	586			AA	;	2000	0323	(	CA 1	999-:	2340	586		19	990	326	
AU	9960	217			A1		2000	0403		AU 1	999-	6021	7		19	9990	326	
EP	1108	068			A1	,	2001	0620		EP 1	999-	9691	21		19	990	326	
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FI,	RO											
JP	2002	5250	77		Т2		2002	0813	,	JP 2	000-	5703	72		19	9990	326	
US 2003125269				A1		2003	0703	1	JS 1	999-:	38389	94		19	9908	326		
PRIORITY APPLN. INFO.:			.:					1	JS 1	998-	98004	4 P	]	P 19	9808	326		
								1	JS 1	999-:	1173	99P	1	P 19	990:	127		
								1	WO 1	999-1	US19	675	1	W 19	9908	326		

AΒ The present invention is directed to isolated nucleic acid mols. encoding pancreatic T-type calcium channels and vectors and host cells comprising such. The invention is further directed to methods and compns. which modulate the expression of pancreatic T-type calcium channels, including antisense. An isolated pancreatic T-type calcium channel protein is provided, as well as antibodies directed to such protein. Pharmaceutical compns. and methods of treatment involving pancreatic T-type calcium channels are also provided. The pharmacol. of Mibefradil action is also discussed and shows that T-type Ca2+ current is more sensitive to mibefradil than the L-type Ca2+ current in pancreatic  $\beta$ -cells. The results also shows that the inhibitory effect of mibefradil on T-type Ca2+ current in pancreatic  $\beta$ -cells results from reversible interaction between the drug and the channel protein. Inhibition of T-type Calcium channels was also shown with a Mibefradil metabolite. Further, it was shown that Streptozotocin induced high basal [Ca2+] inhibits KCL stimulated Ca2+ influx. In addition, it was shown that low voltage-activated Ca2+ current mediates cytokine-induced mouse pancreatic  $\beta$ -cell death. The relationship of this gene to NIDDM (non-insulin-dependent diabetes mellitus) is described. suggest that T-type calcium channels are a primary regulator of resting basal [Ca2+] in  $\beta$ -cells. Applications of antisense DNA are revealed which modulate this gene's expression by blocking translation. Expression of a ribozyme is described which results in decreased expression of this rat pancreatic T-type calcium channel. Oligonucleotide probes for genomic or cDNA library screening are also described along with monoclonal and polyclonal antibodies. Methods for modulation of L-type calcium channels by modifying levels of functional T-type calcium channels is also discussed. Lastly, DNA primers are also mentioned to be used in a PCR reaction for amplification of this gene.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

on STN

ACCESSION NUMBER: 2000292057 EMBASE

TITLE: Identification of elF2By and elF2y as cofactors

of hepatitis C virus internal ribosome entry site-mediated

translation using a functional genomics approach.

AUTHOR: Kruger M.; Beger C.; Li Q.-X.; Welch P.J.; Tritz R.;

Leavitt M.; Barber J.R.; Wong-Staal F.

CORPORATE SOURCE: F. Wong-Staal, Department of Medicine, University of

California, San Diego School of Medicine, 9500 Gilman

Drive, San Diego, CA 92093-0665, United States.

fwongstaal@ucsd.edu

SOURCE: Proceedings of the National Academy of Sciences of the

United States of America, (18 Jul 2000) 97/15 (8566-8571).

ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

LANGUAGE: English SUMMARY LANGUAGE: English

AB The 5'-untranslated region of hepatitis C virus (HCV) is highly conserved, folds into a complex secondary structure, and functions as an internal ribosome entry site (IRES) to initiate translation of HCV proteins. We have developed a selection system based on a randomized hairpin

ribozyme gene library to identify cellular

factors involved in HCV IRES function. A retroviral vector

ribozyme library with randomized target recognition

sequences was introduced into HeLa cells, stably expressing a bicistronic construct encoding the hygromycin B phosphotransferase **gene** and the herpes simplex virus thymidine kinase **gene** (HSV-tk).

Translation of the HSV-tk gene was mediated by the HCV IRES.

Cells expressing ribozymes that inhibit HCV

IRES-mediated translation of HSV-tk were selected via their resistance to both ganciclovir and hygromycin B. Two ribozymes reproducibly conferred the ganciclovir-resistant phenotype and were shown to inhibit IRES-mediated translation of HCV core protein but did not inhibit cap-dependent protein translation or cell growth. The functional targets of these ribozymes were identified as the gamma subunits of human eukaryotic initiation factors 2B (elF2By) and 2 (elF2y), respectively. The involvement of elF2By and elF2y in HCV IRES-mediated translation was further validated by ribozymes directed against additional sites within the mRNAs of these genes. In addition to leading to the identification of cellular IRES cofactors, ribozymes obtained from this cellular selection system could be directly used to specifically inhibit HCV viral translation, thereby facilitating the development of new

L7 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:691208 CAPLUS

antiviral strategies for HCV infection.

DOCUMENT NUMBER: 131:333788

TITLE: Human gene ether-a-go-go potassium channel

polypeptides and polynucleotides, cDNA and amino acid sequences, and biological, therapeutic and diagnostic

uses thereof

INVENTOR(S): Pardo-Fernandez, Luis Angel; Stuhmer, Walter; Beckh,

Synnove; Bruggemann, Andrea; Del Camino

Fernandez-Miranda, Donato; Sanchez Perez, Araceli;

Weseloh, Rudiger

PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Forderung der

Wissenschaften e.V., Germany

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	PATENT NO.				KIN		DATE		i	APP	LIC	CATI	ON 1	NO.		D	ATE	
	9954				A2			1028	ī	MO	199	99-E	EP269	95		1	9990	421
WO	9954 W:	463 CA,			<b>A</b> 3		2000	0420										
		AT,	BE,		CY,	DE,	DK,	ES,	FI,	FR	₹ <b>,</b> G	B,	GR,	IE,	IT,	LU,	MC,	NL,
CA	2323	•			AA		1999	1028	(	CA	199	9-2	23235	571		1	9990	421
EP	1073	738			A2		2001	0207	]	ĒΡ	199	9-9	2073	31		1	9990	421
EP	1073	738			B1		2004	0929										
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	≀, I	T,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	FI															
	2002						2002	0423	· ·	JΡ	200	0-5	4479	95		1	9990	421
AT	2780	17			· E		2004	1015	1	AΤ	199	9-9	2073	31		1	9990	421
US	6638	736			В1		2003	1028	τ	JS	200	0-6	947	77		2	0001	023
US	2003	0777	35		<b>A</b> 1		2003	0424	τ	JS	200	2-1	.8830	8		2	0020	701
US	2003	0873	77		<b>A</b> 1		2003	0508	τ	JS	200	2-1	.8829	96		2	0020	701
US	2003	0873	78		A1		2003	0508	τ	JS	200	2-1	.8834	11		2	0020	701
US	2003	0921	20		A1		2003	0515	τ	JS	200	2-1	.8829	97		2	0020	701
PRIORIT	Y APP	LN.	INFO	. :					I	EΡ	199	8-1	.0726	58	1	A 1	9980	421
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									Ţ	JS	200	0-6	9477	77	1	A3 2	0001	023

The invention relates to novel human gene ether-a-go-go K+ ion AB channel (heag) isoforms, to nucleic acid mols. encoding these isoforms (heag1 and heag2), to expression vectors comprising said nucleic acid mols. and to the use of these vectors in recombinant production of heag. The invention also relates to monoclonal antibodies specifically directed to heag isoforms, and to pharmaceutical compns. and diagnostic kits containing at least one of the above-mentioned components. The present invention further relates to methods for treating or preventing a disease caused by malfunction of heag or by the aberrant expression of the nucleic acid mol. encoding heag. The methods specifically involve administering inhibitors and/or modifying agents that prevent expression of the nucleic acid mol. encoding head and/or that inhibit the function or malfunction of the K+ ion channel. Still further the invention relates to: (1) methods of designing drugs for treating or preventing the above-mentioned disease, (2) methods of inhibiting cell proliferation, (3) methods of prognosing cancer (mammalian carcinoma), neurodegenerative diseases (Alzheimer's disease, Parkinson's disease, lateral amyotrophic sclerosis or multiple sclerosis) and/or psoriasis, and (4) methods of identifying an inhibitor of the function of heag or expression of heag encoding nucleic acid mols. And finally the invention relates to the use of heag in gene therapy. The cDNA sequences as well as the amino acid sequences of heag isoforms are provided. The invention showed the inhibition of human gene eag mRNA expression in EFM cells using a 19-mer antisense phosphorothicate ODN. The invention also showed that human eag gene mRNA is expressed in brain and in several human tumor cell lines including MCF-7, BT-474, EFM-19, COLO-824 and SHSY5Y.

L7 ANSWER 21 OF 25 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN DUPLICATE 6

ACCESSION NUMBER: 1999207845 EMBASE

TITLE: Combinatorial screening and intracellular antiviral

activity of hairpin ribozymes directed

against hepatitis B virus.

AUTHOR: Zu Putlitz J.; Yu Q.; Burke J.M.; Wands J.R.

CORPORATE SOURCE: J.R. Wands, Liver Research Center, 55 Claverick St.,

Providence, RI 02903, United States. JackWandsMD@Brown.edu

SOURCE: Journal of Virology, (1999) 73/7 (5381-5387).

Refs: 35

ISSN: 0022-538X CODEN: JOVIAM

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology

037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

AB A combinatorial screening method has been used to identify hairpin ribozymes that inhibit hepatitis B virus (HBV)

replication in transfected human hepatocellular carcinoma (HCC) cells. A

hairpin ribozyme library (5 x 105 variants)

containing a randomized substrate-binding domain was used to identify accessible target sites within 3.3 kb of full-length in vitro- transcribed HBV pregenomic RNA. Forty potential target sites were found within the HBV pregenomic RNA, and 17 sites conserved in all

four subtypes of HBV were chosen for intracellular inhibition experiments.

Polymerase II and III promoter **expression** constructs for corresponding **hairpin ribozymes** were generated and

cotransfected into HCC cells together with a replication-competent dimer of HBV DNA. Four ribozymes inhibited HBV replication by 80, 69,

66, and 49%, respectively, while catalytically inactive mutant forms of these ribozymes affected HBV replication by 36, 28, 0, and 0%.

These findings indicate that the inhibitory effects on HBV replication were largely mediated by the catalytic activity of the ribozymes

. In conclusion, we have identified catalytically active RNAs by combinatorial screening that mediate intracellular antiviral effects on HBV.

L7 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:88583 CAPLUS

DOCUMENT NUMBER: 130:293203

TITLE: Molecular cloning of mouse glycolate oxidase, high

evolutionary conservation and presence of an

iron-responsive element-like sequence in the mRNA

AUTHOR(S): Kohler, Stefan A.; Menotti, Eric; Kuhn, Lukas C. CORPORATE SOURCE: Swiss Institute for Experimental Cancer Research,

Lausanne, CH-1066, Switz.

SOURCE: Journal of Biological Chemistry (1999), 274(4),

2401-2407

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular

Biology

DOCUMENT TYPE: Journal LANGUAGE: English

AB Iron regulatory proteins (IRPs) control the synthesis of several proteins in iron metabolism by binding to iron-responsive elements (IREs), a hairpin structure in the untranslated region (UTR) of

corresponding mRNAs. Binding of IRPs to IREs in the 5' UTR inhibits translation of ferritin heavy and light chain, erythroid aminolevulinic acid synthase, mitochondrial aconitase, and Drosophila succinate dehydrogenase b, whereas IRP binding to IREs in the 3' UTR of transferrin receptor mRNA prolongs mRNA half-life. To identify new targets of IRPs, we devised a method to enrich IRE-containing mRNAs by using recombinant IRP-1 as an affinity matrix. A cDNA library established from enriched mRNA was screened by an RNA-protein band shift assay. This revealed a novel IRE-like sequence in the 3' UTR of a liver-specific mouse mRNA. The newly identified cDNA codes for a protein with high homol. to plant glycolate oxidase (GOX). Recombinant

protein expressed in bacteria displayed enzymic GOX activity. Therefore, this cDNA represents the first vertebrate GOX homolog. The IRE-like sequence in mouse GOX exhibited strong binding to IRPs at room temperature However, it differs from functional IREs by a mismatch in the middle of its upper stem and did not confer iron-dependent regulation in cells.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 25 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 7

ACCESSION NUMBER: 1999:226778 BIOSIS DOCUMENT NUMBER: PREV199900226778

TITLE: Design, characterization and testing of tRNA3Lys-based

hammerhead ribozymes.

AUTHOR(S): Medina, Maria Fe C.; Joshi, Sadhna [Reprint author]

CORPORATE SOURCE: Department of Medical Genetics and Microbiology, Faculty of

Medicine, University of Toronto, 150 College Street No.

212, Toronto, ON, M5S 3E2, Canada

SOURCE: Nucleic Acids Research, (April 1, 1999) Vol. 27, No. 7, pp.

1698-1708. print.

CODEN: NARHAD. ISSN: 0305-1048.

DOCUMENT TYPE: Article LANGUAGE: English

ENTRY DATE: Entered STN: 17 Jun 1999

Last Updated on STN: 17 Jun 1999

A hammerhead ribozyme targeted against the HIV-1 env coding region was expressed as part of the anticodon loop of human tRNA3Lys without sacrificing tRNA stability or ribozyme catalytic activity. These tRNA-ribozymes were isolated from a library which was designed to contain linkers (sequences connecting the ribozyme to the anticodon loop) of random sequence and variable length. The ribozyme target site was provided in cis during selection and in trans during subsequent characterization. tRNA-ribozymes that possessed ideal combinations of linkers were expected to recognize the cis target site more freely and undergo cleavage. The cleaved molecules were isolated, cloned and characterized. Active tRNA-ribozymes were identified and the structural features conducive to cleavage were defined. selected tRNA-ribozymes were stable, possessed cleavage rates lower or similar to the linear hammerhead ribozyme, and could be transcribed by an extract containing RNA polymerase III. Retroviral vectors expressing tRNA-ribozymes were tested in a human CD4+ T cell line and were shown to inhibit HIV-1 replication. These tRNA3Lys-based hammerhead ribozymes should therefore prove to be valuable for both basic and applied research. Special application is sought in HIV-1 or HIV-2 gene therapy.

L7 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:747594 CAPLUS

DOCUMENT NUMBER: 130:22238

TITLE: Enzymic ribozyme treatment of diseases or cancers

related to expression of c-raf gene

INVENTOR(S): Jarvis, Thale; Matulic-Adamic, Jasenka; Reynolds,

Mark; Kisich, Kevin; Bellon, Laurent; Parry, Tom; Beigelman, Leonid; McSwiggen, James A.; Karpeisky, Alexander; Burgin, Alex; Thompson, James; Workman, Christopher T.; Beaudry, Amber; Sweedler, David

PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc., USA; et al.

SOURCE: PCT Int. Appl., 259 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

P.	PATENT NO.				KIND	1	DATE			AP	PLI	CAT	ON 1	NO.		I	DATE	
		0530 0530					1998	1112						49		1	9980	505
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AU	985	1819	-	•	A1	·	1998	0611	•	AU	19	98-5	5181	9		1	9980	112
AU	729	657 8640 2905 561			B2		2001	0208										
C.F	228	8640			AA		1998	1112		CA	19	98-2	2288	640		1	9980	505
AU	987	2905			A1		1998	1127		AU	19	98-7	7290	5		1	9980	505
AU	749	561			B2		2002	0627										
E	980	424			A2		2000	0223		ΕP	19	98-9	202	99		1	9980	505
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		IE,	FI														•	
JE	200	15256	67		Т2		2001	1211		JΡ	19	98-5	5484	48			.9980	
E	132				<b>A</b> 1													
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		2909			Α		2000										.9990	
	993						1999			AU	19	99-3	3918	8		1	.9990	713
US	630	3773			B1		2001			US	20	000-6	5449	62		2	0000	823
AU	769	175 20289 9465			B2		2004			AU	20	00-5	661	6		2	0000 0000 0010	911
US	200	20289	19		Al		2002			US	20	01-9	96019	92		2	0010	921
US	648	9465			B2		2002									_		
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US	967	3918	01		B2		2004				20					_		000
0.5	200	3918 31252 7815	91		AI		2003			US	20	102-2	://20	03		2	0021	022
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										US	20	01-9	6019	92	1	A1 2	0010	921
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AB This invention relates to identification, synthesis and use of nucleic acid catalysts to cleave RNA species that are required for cellular growth responses. In particular, the invention describes the selection and

function of ribozymes capable of cleaving RNA encoded by c-raf gene. Such ribozymes may be used to inhibit the proliferation of tumor cells in one or more cancers, restenosis, psoriasis, fibrosis and rheumatoid arthritis.

ANSWER 25 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:728548 CAPLUS

DOCUMENT NUMBER: 130:835

TITLE: Intracellular glucocorticoid-induced leucine zipper

proteins as modulators of apoptosis in lymphocytes

INVENTOR(S): Riccardi, Carlo

PATENT ASSIGNEE(S): Applied Research Systems Ars Holding N.V., Neth.

Antilles

SOURCE: PCT Int. Appl., 109 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

<b>P</b> .	PATENT NO.					KINI	D	DATE		4		LICAT				D.	ATE	
W	0	98492	291			A1	_	1998	1105	1		1998-				1	9980	427
		W:	ΑL,	AM,	ΑT,	ΑU,	ΑZ,	BB,	BG,	BR,	BY	, CA,	CH,	CN,	CU,	CZ,	DE,	DK,
			EE,	ES,	FI,	GB,	GE,	GH,	GM,	GW,	HU	, ID,	IL,	IS,	JP,	KE,	KG,	KP,
			KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV	, MD,	MG,	MN,	MW,	MX,	NO,	NZ,
			PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK	, SL,	ТJ,	TM,	TR,	TT,	UA,	UG,
			US,	UZ,	VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG	, KZ,	MD,	RU,	ТJ,	TM		
		RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SZ,	UG,	ZW	, AT,	ΒE,	CH,	CY,	DE,	DK,	ES,
			FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL	, PT,	SE,	BF,	ВJ,	CF,	CG,	CI,
			CM,	GA,	GN,	ML,	MR,	NE,	SN,	TD,	ΤG							
E	Ρ	8843	85			<b>A1</b>		1998	1216		EΡ	1997-	1070	33		1	9970	428
		R:	IT															
C.	Α	22879	906					1998	1105	(	CA	1998-	2287	906		1	9980	427
A	U	9877	593			A1		1998	1124		ΑU	1998-	7759	3		1	9980	427
A	U	7478	69			В2		2002	0523									
E	P	1007	672			A1		2000	0614		ΕP	1998-	9254	88		1	9980	427
		R:	ΑT,		-			ES,	LI,	•		, LV,	•					
J	P	2001				Т2		2001			-	1998-					9980	427
_		68333										2000-					0000	
U	S	2004	19416	50		A1		2004	0930			2003-						
PRIORI	ΤY	APP	LN.	INFO	.:						EΡ	1997-	1070	33	1	A 1	9970	428
							1	WO	<b>1998</b> -1	EP24	90	ı	W 1	9980	427			
										1	US :	2000-	4038	61	1	A2 2	0000	211

AB A protein that plays a role in protecting T-cell from apoptosis induced by anti-CD3 monoclonal antibodies (i.e. Fas-mediated apoptosis) is identified and a cDNA encoding it is cloned. The protein has a leucine zipper and appears to represent a new class of glucocorticoid-induced leucine-zipper related proteins (GILR). A cDNA for the protein was a member of a subtracted library from dexamethasone-induced mouse thymocytes. Sequencing of the clone showed the leucine zipper motif in the gene product. Overexpression of the cDNA protected against the induction of apoptosis by anti-CD3 antibody, but not against glucocorticoid induction. The overexpression appeared to inhibit synthesis of Fas and Fas ligand.

REFERENCE COUNT:

11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 101.87 102.08

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL

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LAST RELOADED: Jan 21, 2005 (20050121/UP).

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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FULL ESTIMATED COST	0.72	102.80
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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L8 7 DUP REM L6 (2 DUPLICATES REMOVED)

=> d ti ab 17 1-7
YOU HAVE REQUESTED DATA FROM FILE 'EMBASE, BIOSIS, MEDLINE, SCISEARCH, CAPLUS' CONTINUE? (Y)/N:y

- L7 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Small interfering RNA libraries and methods of cloning and use
- AB In one aspect, the invention provides a random or semirandom siRNA (encoding) library. Another aspect of the invention pertains to methods for construction of random or semirandom siRNA (encoding) libraries. Another aspect of the invention is vector systems for use in constructing siRNA libraries and/or that can express single siRNAs and siRNA libraries both constitutively and in an inducible fashion. In another aspect, the invention provides a method of using an siRNA library. The siRNA library is introduced into a population of cells. The population of cells then is subjected to a selection process to select a subpopulation of cells exhibiting a different behavioral, biochem., chemical, functional, mol.,

morphol., phenotypic, or phys. property from the remainder of population. Following the selection process, the subpopulation of cells can be isolated, analyzed, and/or cloned as desired. Such anal. of the subpopulation can be identification and sequencing of the siRNA species responsible for the different properties of the subpopulation relative to the remainder of the population. Alternatively, the subpopulation can be further analyzed by genomic, proteomic, and/or cellomic assays. Where such genomic, proteomic, and/or cellomic assays are employed, the method can produce several useful bioinformatics products. Specific siRNAs identified through this process may have direct therapeutic value. The invention claims RNA sequences for four siRNAs that inhibit human estrogen receptor  $\alpha$ . In an example, a human cDNA library is digested into 100-1000 bp fragments using a restriction enzyme and cloned into plasmids having bidirectional transcription driven by flanking, oppositely-oriented T7 promoters. The plasmids also have vaccinia E3L gene cloned in cis with the digested cDNA fragment. The resulting siRNA library is a population of plasmids, each containing a sense and antisense copy of a random 19-mer. In mammalian cells, transcription of the library will produce dsRNA and expression of the E3L protein will. inhibit the interferon response to long dsRNAs and prevent cell death. The endogenous DICER enzyme will process the long dsRNAs into 21-23 bp siRNAs.

- L7 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Method for the synergistic **gene** silencing at both transcription level (using zinc finger protein) and post-transcription level (RNAi technologies), and therapeutic uses
- AB The present invention relates to methods and compns. for regulating a target gene at both transcriptional and post-transcriptional levels. More particularly, it includes in one embodiment, a method for regulating a target gene, which comprises introducing into a cell a zinc finger protein binding to a promoter of the target gene or a DNA encoding said protein, and a RNA mol. binding to an mRNA transcribed from the target gene to inhibit the expression of said target gene. A composition for regulating a target gene comprising the zinc finger protein or a DNA encoding same, and the RNA mol. provide a substantially complete gene regulating effect due to the synergistic effect of the combination of ZFP and RNAi technologies.
- L7 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Protein and cDNA sequences of human and mouse cartilage differentiation inhibiting gene, their therapeutic and diagnostic uses for cartilage related diseases
- AB The present invention provides protein and cDNA sequences of human and mouse cartilage differentiation inhibiting proteins that inhibit type II collagen expression, and their uses in diagnosis, treatment and prevention of diseases associated with cartilage impairments. Using the plasmid CPE43, the cDNA encoding a protein that can inhibit type II collagen expression is cloned from the cDNA library constructed from mouse cell line ATDC5 and human lung fibroblast, and the DNA sequence and the deduced amino acid sequence are determined The protein, the DNA encoding the protein, a recombinant vector containing the DNA, and a transformant containing the recombinant vector are useful in screening for a substance inhibiting or promoting the type II collagen expression.
- L7 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Partially double stranded RNAs with hairpin structures for use in RNA interference without induction of RNA -associated toxicity and their therapeutic uses

- AB Partially double-stranded interfering RNAs that include a hairpin structure are described for use in RNA interference. These interfering RNAs specifically inhibit the expression of target genes in a cell or animal without inducing the toxic effects, such as the RNA stress response, seen with prior art interfering RNAs. These methods can be used to prevent or treat a disease or infection by silencing a gene associated with the disease or infection. The invention also provides methods for identifying nucleic acid sequences that modulate a detectable phenotype, such as the function of a cell, the expression of a gene, or the biol. activity of a target polypeptide.
- L7 ANSWER 5 OF 25 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. ON STN DUPLICATE 1
- TI Identification of cellular cofactors for human immunodeficiency virus replication via a ribozyme-based genomics approach.
- AB Ribozymes are small, catalytic RNA molecules that can be engineered to down-regulate gene expression by cleaving specific mRNA. Here we report the selection of hairpin ribozymes that inhibit human immunodeficiency virus (HIV) replication from a combinatorial ribozyme library . We identified a total of 17 effective ribozymes, each capable of inhibiting HIV infection of human CD4 (+) cells. These ribozymes target diverse steps of the viral replication cycle, ranging from entry to transcription. One ribozyme suppressed HIV integration and transcription by inhibiting the expression of the Ku80 subunit of the DNA-activated protein kinase. Another ribozyme specifically inhibited long terminal repeat transactivation, while two additional ones blocked a step that can be bypassed by vesicular stomatitis virus G-protein pseudotyping. The function of Ku80 in HIV replication and its mechanism of action were further confirmed using short interfering RNA. Identification of the gene targets of these and other selected ribozymes may reveal novel therapeutic targets for combating HIV infection.
- L7 ANSWER 6 OF 25 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. or
- TI Aminoglycoside microarrays to explore interactions of antibiotics with RNAs and proteins
- AB RNA is an important target for drug discovery efforts. Several clinically used aminoglycoside antibiotics bind to bacterial rRNA and inhibit protein synthesis. Aminoglycosides, however, are losing efficacy due to their inherent toxicity and the increase in antibiotic resistance. Targeting of other RNAs is also becoming more attractive thanks to the discovery of new potential RNA drug targets through genome sequencing and biochemical efforts. Identification of new compounds that target RNA is therefore urgent, and we report here on the development of rapid screening methods to probe binding of low molecular weight ligands to proteins and RNAs. A series of aminoglycosides has been immobilized onto glass microscope slides, and binding to proteins and RNAs has been detected by fluorescence. Construction and analysis of the arrays is completed by standard DNA genechip technology. Binding of immobilized aminoglycosides to proteins that are models for study of aminoglycoside toxicity (DNA polymerase and phospholipase C), small RNA oligonucleotide mimics of aminoglycoside binding sites in the ribosome (rRNA A-site mimics), and a large (approximate to 400 nucleotide) group I ribozyme RNA is detected. The ability to screen large RNAs alleviates many complications associated with binding experiments that use isolated truncated regions from larger RNAs. These studies lay the foundation for rapid identification of small organic ligands from combinatorial libraries that exhibit strong and selective RNA

binding while displaying decreased affinity to toxicity-causing proteins.

L7 MEDLINE on STN ANSWER 7 OF 25 DUPLICATE 2

A plasmid-based system for expressing small interfering RNA ΤI libraries in mammalian cells.

BACKGROUND: RNA interference (RNAi) is an evolutionarily AR conserved process that functions to inhibit gene expression. The use of RNAi in mammals as a tool to study gene function has rapidly developed in the last couple of years since the discovery that the function-inhibiting units of RNAi are short 21-25 nt double-stranded RNAs (siRNAs) derived from their longer template. The use of siRNAs allows for gene-specific knock-down without induction of the non-specific interferon response in mammalian cells. Multiple systems have been developed to introduce siRNAs into mammals. One of the most appealing of these techniques is the use of vectors containing polymerase III promoters to drive expression of hairpin siRNAs. However, there are multiple limitations to using hairpin siRNA vectors including the observation that some are unstable in bacteria and are difficult to sequence. RESULTS: To circumvent the limitation of hairpin siRNA vectors we have developed a convergent opposing siRNA expression system called pHippy. We have generated pHippy vectors or expression cassettes that knock down the expression of both reporter and endogenous genes. As a proof of principle that pHippy can be used to generate random siRNA libraries, we generated a small siRNA library against PGL3 luciferase and demonstrated that we could recover functional siRNAs that knock down PGL3 luciferase. CONCLUSIONS: siRNA is a powerful tool to study gene function. We have developed a new vector with opposing convergent promoters for the expression of siRNAs, which can be used to knock down endogenous genes in a high throughput manner or to perform functional screening with random or cDNA-derived siRNA libraries.

=> d ibib 17 1 4 5 7 YOU HAVE REQUESTED DATA FROM FILE 'EMBASE, BIOSIS, MEDLINE, SCISEARCH, CAPLUS' -CONTINUE? (Y)/N:y

ANSWER 1 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:1020024 CAPLUS

DOCUMENT NUMBER:

141:421013

TITLE:

Small interfering RNA libraries

and methods of cloning and use

INVENTOR(S):

Nichols, Mark; Steinman, Richard

PATENT ASSIGNEE(S):

University of Pittsburgh of the Commonwealth System of

Higher Education, USA

SOURCE:

PCT Int. Appl., 73 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	ENT	NO.	KIN	D	DATE			APPL	ICAT	DATE							
WO 2004101788					A2	A2 20041125			1	WO 2	004-	20040510					
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PRIORITY APPLN. INFO.:
                                            US 2003-469169P
                                                                P 20030509
    ANSWER 4 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                        2004:101279 CAPLUS
                        140:158524
                        Partially double stranded RNAs with
```

DOCUMENT NUMBER:

TITLE: hairpin structures for use in RNA interference without induction of RNA

-associated toxicity and their therapeutic uses

INVENTOR(S): Pachuk, Catherine J.; Satishchandran, C.; Chopra,

Maninder; Shuey, David PATENT ASSIGNEE(S): Nucleonics, Inc., USA SOURCE: PCT Int. Appl., 174 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO.					D	DATE			APPL	ICAT	DATE							
	WO 2004011624			A2		2004		1	WO 2	003-	20030731								
WO	VO 2004011624				C2		2004	0408											
WO	O 2004011624			<b>A3</b>		20041209													
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ANSWER 5 OF 25 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 1

ACCESSION NUMBER: 2004493962 EMBASE

Identification of cellular cofactors for human TITLE: immunodeficiency virus replication via a ribozvme

-based genomics approach.

AUTHOR: Waninger S.; Kuhen K.; Hu X.; Chatterton J.E.; Wong-Staal

F.; Tang H.

CORPORATE SOURCE: H. Tang, Department of Biological Sciences, Biology Unit 1,

Florida State University, Tallahassee, FL 32306-4370,

United States. tang@bio.fsu.edu

SOURCE: Journal of Virology, (2004) 78/23 (12829-12837).

Refs: 35

ISSN: 0022-538X CODEN: JOVIAM

COUNTRY: United States DOCUMENT TYPE: Journal; Article FILE SEGMENT: 004 Microbiology

> 026 Immunology, Serology and Transplantation

LANGUAGE: English SUMMARY LANGUAGE: English

ANSWER 7 OF 25 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2004256536 MEDLINE PubMed ID: 15119963 DOCUMENT NUMBER:

A plasmid-based system for expressing small interfering TITLE:

RNA libraries in mammalian cells.

Kaykas Ajamete; Moon Randall T AUTHOR:

Howard Hughes Medical Institute, Department of CORPORATE SOURCE:

Pharmacology, and Center for Developmental Biology,

University of Washington School of Medicine, Seattle, WA

98195,. USA.akaykas@u.washington.edu

BMC cell biology [electronic resource], (2004 Apr 30) 5 (1) SOURCE:

Journal code: 100966972. ISSN: 1471-2121.

England: United Kingdom PUB. COUNTRY:

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200406

ENTRY DATE: Entered STN: 20040525

> Last Updated on STN: 20040602 Entered Medline: 20040601

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8 SMALL (W) INTERFER? (W) RNA (W) LIBRAR?

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L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1020024 CAPLUS

DOCUMENT NUMBER: 141:421013

Small interfering RNA TITLE:

libraries and methods of cloning and use

Nichols, Mark; Steinman, Richard INVENTOR(S):

University of Pittsburgh of the Commonwealth System of PATENT ASSIGNEE(S):

Higher Education, USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PRIORITY APPLN. INFO.:
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L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                            2004:80856 CAPLUS
                            140:140740
DOCUMENT NUMBER:
                            dual pol III promoter cassette for transcription of
                            small interfering RNA (siRNA) library and uses
INVENTOR(S):
                            Li, Henry; Chatterton, Jon E.; Ke, Ning; Wong-Staal,
                            Flossie
PATENT ASSIGNEE(S):
                            Immusol, Inc., USA
                            PCT Int. Appl., 66 pp.
                            CODEN: PIXXD2
DOCUMENT TYPE:
                            Patent
                            English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
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     US 2004146858
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PRIORITY APPLN. INFO.:
                                                  US 2002-398915P
                                                                         P 20020724
L10 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
                      2004:274067 BIOSIS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                      PREV200400274357
                      Small interfering RNA production by enzymatic engineering
                      of DNA (SPEED).
AUTHOR(S):
                      Luo, Biao; Heard, Amanda D.; Lodish, Harvey F. [Reprint
                      Author]
                      Whitehead Inst Biomed Res, 9 Cambridge Ctr, Cambridge, MA,
CORPORATE SOURCE:
                      02142, USA
                      lodish@wi.mit.edu
                      Proceedings of the National Academy of Sciences of the
                      United States of America, (April 13 2004) Vol. 101, No. 15,
                      pp. 5494-5499. print.
                      ISSN: 0027-8424 (ISSN print).
DOCUMENT TYPE:
                      Article
LANGUAGE:
                      English
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L10 ANSWER 4 OF 6 MEDLINE on STN

Entered STN: 2 Jun 2004

Last Updated on STN: 2 Jun 2004

TITLE:

SOURCE:

TITLE:

SOURCE:

ENTRY DATE:

DUPLICATE 1

ACCESSION NUMBER: 2004256536 **MEDLINE** DOCUMENT NUMBER: PubMed ID: 15119963

TITLE: A plasmid-based system for expressing small

interfering RNA libraries in

mammalian cells.

AUTHOR: Kaykas Ajamete; Moon Randall T

Howard Hughes Medical Institute, Department of CORPORATE SOURCE:

Pharmacology, and Center for Developmental Biology, University of Washington School of Medicine, Seattle, WA

98195,. USA.akaykas@u.washington.edu

SOURCE: BMC cell biology [electronic resource], (2004 Apr 30) 5 (1)

Journal code: 100966972. ISSN: 1471-2121.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

Priority Journals FILE SEGMENT:

200406 ENTRY MONTH:

ENTRY DATE: Entered STN: 20040525

> Last Updated on STN: 20040602 Entered Medline: 20040601

L10 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

DUPLICATE 2

ACCESSION NUMBER: 2004:320712 BIOSIS DOCUMENT NUMBER: PREV200400321938

A plasmid-based system for expressing small TITLE:

interfering RNA libraries in

mammalian cells.

AUTHOR(S): Kaykas, Ajamete; Moon, Randall T. [Reprint Author]

CORPORATE SOURCE: Howard Hughes Med InstDept Pharmacol, Univ Washington,

Seattle, WA, 98195, USA

akaykas@u.washington.edu; rtmoon@u.washington.edu

BMC Cell Biology, (April 30 2004) Vol. 5, No. April 30. SOURCE:

print.

ISSN: 1471-2121 (ISSN online).

DOCUMENT TYPE: Article LANGUAGE: English

Entered STN: 21 Jul 2004 ENTRY DATE:

Last Updated on STN: 21 Jul 2004

L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

2003:614194 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 139:144419

TITLE: Development of siRNA libraries by in vitro dicing and

optimized efficient expression vectors for siRNAs in

mammalian cells

Kawasaki, Hiroaki; Miyagishi, Makoto; Taira, Kazunari AUTHOR(S):

Grad. Sch. Eng., The Univ. Tokyo, Japan CORPORATE SOURCE:

SOURCE: Tanpakushitsu Kakusan Koso (2003), 48(11, Zokango),

1638-1645

CODEN: TAKKAJ; ISSN: 0039-9450

Kyoritsu Shuppan PUBLISHER:

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese